Remarks

A. Status of Claims

No claim amendments are being presented. Pending claims 19–35 are listed in Appendix A.

B. Section 102 Rejections

Claims 19, 20, 22, 24, 25, 27, 28, 30, and 31 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,922,537 ("Ewart"). Applicants respectfully traverse.

1. Ewart does not anticipate independent claim 19

Independent claim 19 recites an engineered microparticle having a first dielectric property and a complex having a second dielectric property. The complex is detected "by distinguishing between the first and second dielectric properties." *See* claim 19.

Ewart does not disclose or suggest detecting a complex by distinguishing between a dielectric property of a microparticle and a dielectric property of a complex. Rather, a reading of Ewart reveals that it detects a complex by distinguishing a difference in global device capacitance arising from a complex being added to, or taken away from, a test surface of a biosensor. Multiple passages of Ewart reinforce this conclusion. For example, consider the following:

> In accordance with this invention, particle reporters are provided as labelling entities for use in a variety of biosensors. The particle reporters greatly enhance the sensitivity of the biosensors and are capable of detecting the addition or substraction of a single particle reporter to or from the test surface. [col. 3, line 66 - col. 4, line 4] (emphasis added).

> As shown in FIG. 1C the second analyte 22 in the sample has competed with the first analyte entities 12 to displace the reporter particles 18 away from the test surface 10. Such displacement of the reporter particles from the test surface results in a measurable difference, hence determining through suitable controls of the and biosensors, both a qualitative and quantitative measure of the analyte present in the sample. [col. 4, lines 35-42] (emphasis added).
>
> The materials useful as capacitance particle reporters which combine with recognition molecules or analyte entities are those which will alter the electrical reactance of the test surface. That is, these materials, if distributed as a finely divided powder on the test surface, alter the dielectric, conductive or the magnetic properties of the surface. The advantage of this invention resides in using particles which are detectable in very small quantities by very sensitive but well developed and readily available electrical components. [col. 9, lines 13-21] (emphasis added).
>
> When the sample is introduced to the test surface, the analyte molecules 114 compete with the analyte entities 108 for the recognition molecule site of the phage 110. This competition forms a complex of the phage particles 110 by virtue of their recognition molecules 112 binding to the analyte 114. Such competition removes the phage particles 110 from the test surface. By removal of such analyte particles from the test surface, the capacitance of the device has changed and hence, a measure of the amount of analyte in the sample can be detected by use for example, of the biosensors of FIGS. 10 and 11. [col. 17, lines 7-16] (emphasis added).

Thus, it is clear that Ewart is exploiting the difference in global capacitance associated with a test surface of a biosensor to determine the presence of a complex, *not* the difference in dielectric properties of a microparticle and its associated complex. In particular, Ewart measures a change in capacitance as particles are removed from, or added to, a test surface. By noting small changes in capacitance, Ewart infers the presence of analytes. Utilizing global capacitance differences associated with a test surface of a biosensor, however, is far different than relying on differences between dielectric properties of a microparticle and its associated complex.

Accordingly, Ewart does not disclose (nor does it suggest) subject matter of independent claim 19. Applicants therefore assert that claim 19 and its dependent claims are allowable, and they respectfully request removal of the current rejection.

Applicants anticipate that the Office may reason that changes in capacitance in Ewart can be traced back to differences in dielectric properties and, thus, the current rejection is justified. Such an argument, however, would be faulty and would not render the claims anticipated (or obvious) because the dielectric properties giving rise to the measurable change in capacitance in Ewart are *not* the dielectric properties of a microparticle versus the dielectric properties of its associated complex. Rather, the dielectric properties accountable for the measurable change in capacitance in Ewart are those of microparticles and a buffer medium (*e.g.*, water). For example, at columns 13–14, Ewart explains that the measurable change in capacitance arises because of differences in dielectric constants of particles versus the dielectric constant of water. *See* , *e.g.*, col. 13, lines 29–67. Consider the following passage of Ewart, in which K_d refers to the dielectric constant of particles while K_w refers to the dielectric constant of water:

> The thickness of the water layer is the same as that of the dielectric particle layer with which it exchanges. Thus it can be seen from equations 12A and 12B that the change [in capacitance] is determined exclusively by the change in dielectric constant Kd to Kw in the complexing layer. [col. 13, lines 60-63] (emphasis added).

Thus, Ewart discloses that its mechanism for capacitance changes is determined "exclusively" by the differences in dielectric properties of water versus particles. This, however, does not and cannot amount to a disclosure or suggestion of detection by distinguishing between dielectric properties of a particular microparticle and its associated complex, as recited in independent claim 19.

In fact, it can be argued that Ewart *teaches away* from the present invention. At column 14, lines 21–38, Ewart lists several purported advantages. Advantage #1 (lines 22–25) reinforces the discussion above because it notes that the dielectric constant of a label/tag should be chosen to be optimally different than that of the *buffer medium* (*e.g.*, water). Advantage #2 (lines 26–32) suggests that a dielectric label/tag be large so that more buffer particles (*e.g.*, water particles) will be required to replace it (and, hence, a larger capacitance change may result). Advantage #3 (lines 33–38) suggests that a dielectric label/tag be selected so that its dielectric properties wash out or dominate those of an associated complex so that inherent variations in dielectric properties are minimized. Each of these purported advantages, however, teaches away from considering differences in dielectric properties of microparticles and associated complexes for detection.

In sum, Ewart clearly does not disclose or suggest the features of independent claim 19. For at least the reasons given above, Applicants respectfully assert that claim 19 is in condition for allowance. For at least the same reasons, all claims depending from claim 19 are allowable as well. Applicants request removal of the current rejection so that the claims can pass to issuance.

2. Ewart does not anticipate independent claim 24

Independent claim 24 recites, in part, associating an engineered microparticle with a target analyte to form a complex and manipulating the complex using dielectrophoresis.

Ewart does not disclose or suggest such features. The Examiner appears to rely solely on the following passage of Ewart in support of the current rejection:

> Phage particles may be selected which have the desired dielectric constant usually of about 3, for use in this invention as reporter particles in a capacitance biosensor. Considering that water has a dielectric constant about 81, the dielectric constant of a phage renders it quite useful in this invention. Phages behave as very high molecular weight proteins in solution and therefore can be caused to move in an electrophoretic field--this being advantageous for separation from the surface of the capacitor. [col. 11, lines 22-31] (emphasis added).

Independent claim 24 requires manipulation of a complex (including a microparticle having a conductive core and an insulating coating layer) using *dielectrophoresis*. The particular, disclosed phage of Ewart does not appear to meet or suggest claim 24's recitation of a microparticle having a conductive core and an insulating coating layer. Further, even if such a phage were to meet this recitation, the disclosed "electrophoretic field" of Ewart does not amount to a disclosure or even a suggestion of manipulation by *dielectrophoresis*. Electrophoresis and dielectrophoresis are different, and disclosure of one does not suggest the other. The Office is respectfully directed to an appropriate dictionary or to the specification at page 33, line 27 – page 34, line 12 for a general explanation.

In sum, Ewart does not disclose or suggest the features of independent claim 24. Applicants respectfully assert that claim 24 is in condition for allowance. All claims depending from claim 24 are allowable for at least the same reasons. Applicants therefore request removal of the current rejection so that the claims can pass to issuance.

B. Section 103 Rejections

Claims 21, 26, and 29 stand rejected under 35 U.S.C. § 103 as being obvious over Ewart. Applicants respectfully traverse and assert that the dependent claims are allowable for at least the reasons given for independent claims 19 and 24.

D. Allowable subject matter

Applicants appreciate and acknowledge the Examiner's indication that claims 23 and 32–35 contain allowable subject matter. However, for the reasons given above, it is respectfully submitted that each of the other pending claims also contains subject matter patentably distinct from the art.

Petition for Extension of Time

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for an extension of time of one month up to and including May 16, 2003 in which to respond to the Office Action dated 16 January 2003. A check for the $55.00 extension fee is enclosed. Should any additional fees be required for any reason, or should an over-payment be included, the Commissioner is authorized to deduct or credit Fulbright & Jaworski Deposit Account No. 50-1212/UTXC:626US.

Conclusion

Applicants believe this response fully and completely addresses all outstanding issues for this application. Applicants respectfully submit that the rejections of all pending claims should be withdrawn. The pending claims should be allowed to pass to issuance because they are free of the cited art. If the Examiner has any questions or wishes to discuss this case further, please do not hesitate to contact the undersigned attorney.

Additionally, if the Examiner intends to maintain any of the rejections discussed in this response, the courtesy of a telephone conference between the Examiner, the Examiner's supervisor, and the undersigned attorney is respectfully requested in advance.

Respectfully submitted,

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Appendix A

19. A method for detecting a complex within a sample, the method comprising:

admixing with the sample an engineered microparticle having a first dielectric property and comprising a conductive core, an insulating layer having a thickness sufficient to render the microparticle maneuverable by dielectrophoresis, and a linking element;

associating the engineered microparticle with a target analyte to form the complex, the complex having a second dielectric property; and

detecting the complex by distinguishing between the first and second dielectric properties.

20. The method of claim 19, wherein the sample comprises blood, urine, saliva, amniotic fluid, biopsy, cell suspension, cell lysate, chromatographic fraction, or conditioned media.

21. The method of claim 19, wherein the sample comprises water, food, food processing, food distribution, mineral, or ore.

22. The method of claim 19, wherein the linking element comprises an antibody, single chain antibody, peptide, hormone, nucleic acid sequence, therapeutic drug, antibiotic, or a chemically-reactive compound.

23. The method of claim 19, wherein the insulating layer comprises one or more self-assembled monolayer layers.

24. A method for manipulating a complex in a sample, the method comprising:

admixing with the sample an engineered microparticle comprising a conductive core, an insulating layer coating the conductive core and having a thickness sufficient to render the engineered microparticle maneuverable by dielectrophoresis, and a linking element;

associating the engineered microparticle with the target analyte to form the complex; and

manipulating the complex using dielectrophoresis.

25. The method of claim 24, wherein the sample comprises blood, urine, saliva, amniotic fluid, biopsy, cell suspension, cell lysate, chromatographic fraction, or conditioned media..

26. The method of claim 24, wherein the sample comprises water, food, food processing, food distribution, mineral, or ore..

27. The method of claim 24, wherein the manipulating comprises sorting.

28. The method of claim 24, wherein the manipulating comprises separating.

29. The method of claim 24, wherein the manipulating comprises purification of the sample.

30. The method of claim 24, wherein the manipulating comprises trapping.

31. The method of claim 24, wherein the linking element comprises an antibody, single chain antibody, peptide, hormone, nucleic acid sequence, therapeutic drug, antibiotic, or a chemically-reactive compound.

32. The method of claim 24, wherein the insulating layer comprises one or more self-assembled monolayer layers.

33. A method for identifying one or more complexes within a sample, the method comprising:

admixing with the sample a plurality of engineered microparticles, each microparticle having a different dielectric property;

associating the plurality of engineered microparticles with one or more target analytes to form one or more complexes; and

identifying the one or more complexes by distinguishing between the different dielectric properties.

34. The method of claim 33, wherein each the plurality of engineered microparticles comprise a conductive core and an insulating layer.

35. The method of claim 34, wherein the insulating layer comprises one or more self-assembled monolayer layers.